UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,682	05/09/2006	Yohei Okada	03327.2346	3661

22852 7590 10/29/2007

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
901 NEW YORK AVENUE, NW
WASHINGTON, DC 20001-4413

EXAMINER	
EBRAHIM, NABILA G	

ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
10/29/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,682	OKADA ET AL.	
	Examiner	Art Unit	
	Nabila G. Ebrahim	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 8-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 8-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of Applicant's remarks and amendments to the claims dated 7/31/07 is acknowledged.

Status of Claims

Claims 1-4 and 8-13 are pending in the application.

Claim 1 was amended.

Claims 5-7 were canceled.

Claims 8-13 are new.

Status of Office Action: Final.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-4, and 8-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 as amended recites " a sustained release composition", as understood in the art "sustained release" is a way of formulating a medicine so that it is released into the body steadily, over a long period of time, thus reducing the dosing frequency. The claims also recite a release profile of the whole drug between 2-24 hours or 3-24 hours. It is not understood how can the drug be released in 2 hours or 3 hours and is still considered a sustained release. This renders the claim ambiguous.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. In view of amendments to claims, the rejection of claims 1-4, and 7 under 35 U.S.C. 102(b) as being anticipated by M. Suzuki et al. Effects of (-)-S-2,8-dimethyl-3-methylene-1-oxa-8-azaspiro[4,5]decane L- tartrate monohydrate (YM796), a novel muscarinic agonist, on disturbance of passive avoidance learning behavior in drug-treated and senescence-accelerated mice, Volume 275, Issue 2, pp. 728-736, 11/01/1995 is herein withdrawn.

2. In view of the amendments to the claims, the rejection of claims 1, 2 and 7 under 35 U.S.C. 102(b) as being anticipated by Tsukamoto Shin-Ichi WO 9220683 (hereinafter "Shin") is herein withdrawn.

1. Claims 1, 3-4, and 8-12 remain rejected under 35 U.S.C. 102(b) as being anticipated by Brann et al. US 6528529 (hereinafter Brann).

Brann teaches compounds with activity on muscarinic receptors. Brann's compounds are the same as the instant application recitation (col. 9, lines 4-6) and discloses that the preparation can be sustained-release (col. 12, lines 61+) and that the unit dosage forms can be in the form of tablets, pills, capsules, powders, granules, elixirs, tinctures, syrups and emulsions, sterile parenteral solutions or suspensions, aerosol or liquid sprays, drops, ampoules, auto-injector devices or suppositories. Note that all these forms usually include carriers.

Regarding the amendments to claim 1, Brann teaches the use of PEG (col. 13, line 27) and polyvinyl pyrrolidone (col. 14, line 3). Since same compounds have same properties, the Examiner assumes that the release profile recited in claims 1 and 8-10 is expected to be the same.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

2. Claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brann et al. US 6528529 (hereinafter Brann) in view of any of M. Suzuki et al. Effects of (-)-S-2,8-dimethyl-3-methylene-1-oxa-8-azaspiro[4,5]decane L- tartrate monohydrate (YM796), a novel muscarinic agonist, on disturbance of passive avoidance learning behavior in drug-treated and senescence-accelerated mice, Volume 275, Issue 2, pp. 728-736, 11/01/1995 (hereinafter Suzuki), or Tsukamoto Shin-Ichi WO 9220683 (hereinafter "Shin") and further in view of Sako et al. US 6699503 (Sako).

Brann teaches compounds with activity on muscarinic receptors. Brann's compounds are the same as the instant application recitation (col. 9, lines 4-6) and discloses that the preparation can be sustained-release (col. 12, lines 61+) and that the unit dosage forms can be in the form of tablets, pills, capsules, powders, granules, elixirs, tinctures, syrups and emulsions, sterile parenteral solutions or suspensions, aerosol or liquid sprays, drops, ampoules, auto-injector devices or suppositories. Note that all these forms usually include carriers.

Brann is deficient in the sense that he did not disclose the tartrate salt of the compound.

Shin teaches the compound (-)-(S)-2,8-Dimethyl-3-methylene-1-oxa-8-azaspiro[4,5]decane L-tartrate having a storage stability superior to that of other salts and being applicable as a medicine (abstract) and also has a selective affinity for the muscarinic acetylcholine receptor. The hydrochloride, fumarate, maleate and di-p-toluoyl-D-tartrate salts of the compound can be utilized in the treatment of diseases. Note that the "treatment of tear and salivary fluid drying" is the intent of use of the composition, which is not considered of weight in the patentability of the instant claims because the prior art composition would have been inherently able to achieve the same use with success. However, it is also noted that it is within the muscarinic agonist effect of the compound to enhance the secretion of lacrimal and salivary glands.

As the title shows, Suzuki teaches the effects of the compound taught in the instant claims. The reference discloses that the compound is a novel muscarinic agonist, and has an effect on disturbance of passive avoidance learning behavior in drug-treated and senescence-accelerated mice. Muscarinic action of the autonomic nervous system is well known to people skilled in the art (see the attached document that describes the muscarinic activity of the autonomic nervous system, page 3). One of these activities is having anti-drying effect on eyes and the mouth.

Note that the effects of the drug and its mechanism of action recited in claims 3, and 4 are inherent properties of the drug.

Suzuki, and Shin disclosed the use of the L-tartrate required by instant claim 2.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to produce 2,8-dimethyl-3-methylene-1-oxa-8-azaspiro[4,5]decane in a sustained-release form to prolong the action of the compound on lacrimal and salivary glands as

disclosed by Brann and produce its tartrate salt because Shin discloses that the L-tartrate has a superior storage stability (abstract).

None of the references teach the use of polyethylene oxide as a polymer for the sustained release formulation.

Sako teaches an invention provides a hydrogel-type sustained-release preparation capable of satisfactorily releasing a drug. The preparation comprising (1) at least one drug, (2) an additive which insures a penetration of water into the core of the preparation and (3) a hydrogen-forming polymer. The formulation provides a steady sustained release effect (abstract). Sako teaches that among hydrogel polymers that are used in sustained-release polymers is polyethylene oxide (PEO) and describes molecular weights and viscosity of the polymer (col. 4, lines 59+ bridging to col. 5, lines 1+). Sako discloses different polymers, however, the reference teaches that the preferred polymer is a PEO and the reference also show how to control the release in a specific time and gives an example disclosing that a release if more than 12 hours, is required, a polymer having a higher molecular weight, preferably an average molecular weight of not less than $2x10^6$ or a higher viscosity, preferably a viscosity of not less than 3000 cps at a concentration of 1% in water at 25°C., is preferable (col. 5, lines 21-28).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine Sako's disclosure of polyethylene oxide preferred use in sustained-release formulations to the combination of Brann and Suzuki or Shin to produce a sustained release formulation comprising 2,8-dimethyl-3-methylene-1-oxa-8-azaspiro[4,5]decane and adjust the molecular weight according to amount of release needed for the patients and to prolong the action of the compound on lacrimal and salivary glands, the motivation would be the disclosure of Sako that PEO is the preferred polymer to achieve these

results. The skilled artisan would have excellent expectation of having a pharmaceutical composition for the treatment of tear and salivary fluid drying.

Response to Arguments

3. Applicant's arguments filed 7/31/07 have been fully considered but they are not persuasive. Applicant argues that Brann does not teach a formulation comprising a sustained release pharmaceutical carrier and wherein the release rate of the active ingredient from the composition is from about 4 percent per hour to about 50 percent per hour.

This was not found persuasive because Brann did disclose compound that can be formulated as a sustained release comprising a polymer such as polyvinylpyrrolidone or polyethylene glycol and though the reference does not recite the hour profile release as disclosed in the instant claims, it is noted that since the reference used the same compounds, the release profile is expected to be the same unless Applicant provides reasons why would the release of the instant formulation would be different.

4. Applicant's arguments with respect to claims 1-4 and 8-13 have been considered but are moot in view of the new ground(s) of rejection. Applicant's main arguments are based on the new amendments to claims, which were properly rejected by introducing Sako et al. US 6699503 to the prior art of record in the 35 USC § 103.

Conclusion

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nabila G. Ebrahim whose telephone number is 571-272-8151. The examiner can normally be reached on 8:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nabila Ebrahim
3/13/07

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER